

K965053

Attachment C

Summary of Safety and Effectiveness

NOV 21 1997

Submitter Information (21 CFR 807.92(a)(1))

Submitter: Becton Dickinson Immunocytometry Systems
2350 Qume Drive
San Jose, CA 95131-1807

Contact: Anna Longwell, Esq.
Director, Regulatory Affairs - Corporate
(408) 954-2254

Summary date: November 18, 1997

Name of Device and Classification (21 CFR 807.92(a)(2))

Name: Becton Dickinson TriTEST™ reagent CD3 FITC/CD4 PE/CD45 PerCP;
TRUCOUNT™ Absolute Count Tubes

Classification: Class II

Predicate Device (21 CFR 807.92(a)(3))

The BDIS TriTEST™ CD3/CD4/CD45 reagent with TRUCOUNT Absolute Count Tubes is substantially equivalent to the BDIS FACSCount system cleared in K933486.

Description of the Device (21 CFR 807.92(a)(4))

The BDIS TriTEST CD3 fluorescein isothiocyanate (FITC)/CD4 phycoerythrin (PE)/CD45 peridinin chlorophyll protein (PerCP) reagent is a three-color, direct immunofluorescence reagent for identifying and enumerating percentages of T lymphocytes (CD3+) and T-helper (CD3+CD4+) cells in erythrocyte-lysed whole blood (LWB). When used with TRUCOUNT Absolute Count Tubes, the product will yield absolute counts in cells/μL. The Becton Dickinson TriTEST/TRUCOUNT system for immunophenotyping consists of a flow cytometer (either from BDIS or from another manufacturer), conjugated monoclonal reagent (TriTEST CD3 FITC/CD4 PE/CD45 PerCP) and TRUCOUNT Absolute Count Tubes.

The process to obtain lymphocyte subset percentages includes: 1) obtaining a whole blood sample, 2) cell-surface antigen staining with three-color monoclonal antibody reagents, 3) erythrocyte lysis, and 4) flow cytometric acquisition and analysis of list mode data. Analysis involves computing the ratio of reagent-positive events (CD3+CD4+) to the CD45 positive events, and expressing the ratio as a percentage.

Summary of Safety and Effectiveness

To obtain absolute counts, the TriTEST reagent and whole blood are added directly to an Absolute Count Tube prior to lysis. The remaining process, until analysis, is identical to that for percentages. Analysis for absolute counts requires that an additional region, the bead region, be identified and the events in this region counted. The proportion of reagent positive events to bead events (P) is computed. The absolute count is $P \times (\text{beads/pellet}) / (\text{volume of blood sample})$.

When monoclonal antibody reagents are added to human whole blood, the fluorochrome-labeled antibodies bind specifically to antigens on the surface of leucocytes, thus identifying lymphocyte populations. The patient blood sample is added to the counting bead pellet and is treated with fluorochrome-labeled antibodies and the erythrocytes are lysed with FACS® Lysing Solution. The flow cytometer is set up so that cell populations for most samples occupy approximately the same region of fluorescence space. The sample is then introduced into the flow cytometer and the stained cells and beads fluoresce when excited by a laser beam.

The three-color reagent permits identification of lymphocyte subsets using fluorescence gating instead of forward scatter gating. This three-color reagent allows direct gating on the CD45-positive population using a combination of fluorescence and side scatter parameters. By gating on the CD45-positive population, a maximum number of lymphocytes may be captured in the gate and non-lymphocyte contamination may be minimized.

Intended Use (21 CFR 807.92(a)(5))

For in vitro diagnostic use to identify and enumerate percentages and absolute counts of CD3+ and CD3+CD4+ lymphocytes in blood.

Indications for Use

- For use with any flow cytometer equipped with a 488 nm laser and capable of detection in the ranges: 515-545 nm, 562-607 nm, and > 650 nm
- For use with erythrocyte-lysed peripheral whole blood
- For use with or without an isotype control
- To characterize and monitor some forms of autoimmune disease
- To characterize and monitor some forms of immunodeficiency disease, such as in HIV-infected individuals

Clinical Utility

The determination of CD3+ and CD3+CD4+ lymphocytes has been found useful in monitoring some forms of immunodeficiency and autoimmune disease.

Summary of Safety and Effectiveness

Comparison to Predicate Device (21 CFR 807.92(a)(6))

The three-color reagent is substantially equivalent to the predicate BDIS FACSCount System in that they share the same intended uses and similar methodologies. Results demonstrate that the products yield essentially equivalent performance characteristics. Both tests are antibody-dependent, in vitro diagnostic assays to identify T lymphocytes (CD3+) and helper/inducer (CD3+CD4+) T-lymphocyte subsets. The products differ in the steps used to determine analysis gates to identify the lymphocyte population.

Performance Data (21 CFR 807.92(b)(2))

Performance of the product was established by testing at Cleveland Clinic, Johns Hopkins Hospital, Institute of Tropical Medicine, University of North Carolina, and at Becton Dickinson Immunocytometry Systems laboratories in San Jose, California.

Several studies were performed:

- Accuracy was determined by comparison to the FACSCount system. Absolute counts for CD3+ were obtained from 197 (152 abnormal and 45 normal) donors. Absolute counts for CD3+CD4+ were obtained from donors; data for CD3+CD4+ was grouped according to range of number of cells. Accuracy data demonstrated the TriTEST/TRUCOUNT product's equivalence to FACSCount. Additionally, a subset of the accuracy study data was analyzed for percent CD3+ and percent CD4+ first using a control to set markers and then using only the stained sample to set quadrant markers. Data indicated that the reagent may be used with or without an isotype control.
- Reference range studies were performed. The reference range for CD3+ and CD3+CD4+ lymphocytes was a function of sex and site. For CD3+ lymphocytes, within the male population, it was also a function of age. Each site must determine its own reference range.
- A stability study was conducted to assess the time effect relating to age of blood (time-from-draw) and the time effect relating to the age of the stain (time-from-sample preparation), as well as the combined effect of both. Stability was determined for both percentages and absolute counts. Stability was determined for whole blood samples at 0, 24, 48 and 72 hours post draw. Additionally, stability was measured for stained samples at 0 and 24 hours from time of staining. A combination of the two, time from draw plus time from sample preparation was studied. Results indicated that either 1) staining the samples within 24 hours of draw and analyzing samples within 24 hours of staining or alternatively, 2) staining the samples with 48 hours of draw and analyzing them within 6 hours is recommended.

Summary of Safety and Effectiveness

- Within-specimen reproducibility was performed at BDIS; 10 replicates from 1 high, 1 medium, and 1 low (with respect to CD3+ and CD3+CD4+ lymphocytes) were assessed. Within-specimen reproducibility was also performed at 3 clinical sites; 3 aliquots from each donor (n=94 for CD3+ and n=80 for CD3+CD4+) were assessed. Results demonstrated acceptable within-sample reproducibility.
- Linearity was determined using blood samples from 3 normal donors diluted to 5 concentrations, ranging from 16,700 to 200 lymphocytes/ μ L and from 31,000 to 2,500 WBC/ μ L. Results indicate a linear response over this range.
- Cross reactivity of these clones is reported in the literature. Conjugation and product formulation have not changed their specificity.
- Results from a cross platform reproducibility study indicated 1) for percentage results the reagent may be used with flow cytometers not made by Becton Dickinson 2) for determining absolute counts using TriTEST reagent with TRUCOUNT Absolute Count Tubes, there was a small (<20%) non-zero bias, but good correlation between results on a Becton Dickinson flow cytometer versus a Coulter cytometer was observed. Therefore, users will be advised that they must validate performance characteristics for absolute counts.

Performance Data - Conclusions (21 CFR 807.92(b)(3))

The results of the clinical studies demonstrate that the device is as safe and effective as the predicate device.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ms. Anna Longwell, Esq.
Director, Regulatory Affairs - Corporate
Becton Dickinson Immunocytometry Systems
2350 Qume Drive
San Jose, California 95131-1807

NOV 21 1997

Re: K965053
Trade Name: Becton Dickinson TriTEST™ Reagent CD3 FITC/CD4
PE/CD45 PerCP; TRUCOUNT™ Absolute Count Tubes
Regulatory Class: II
Product Code: GKZ
Dated: August 28, 1997
Received: September 2, 1997

Dear Ms. Longwell:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

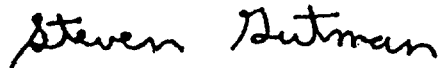
Page 2

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Attachment A
TriTEST CD3/CD4/CD45 with TRUCOUNT Control Beads & Absolute Count Tubes
K965053

Indications for Use Statement

- For use with any flow cytometer equipped with a 488 nm laser and capable of detection in the ranges: 515-545 nm, 562-607 nm, and > 650 nm
- For use with erythrocyte-lysed peripheral whole blood
- For use with or without an isotype control
- To characterize and monitor some forms of autoimmune disease
- To characterize and monitor some forms of immunodeficiency disease, such as in HIV-infected individuals

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)



(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number _____

Prescription Use_____
(Per 21 CFR 801.109)

OR

Over-The-Counter Use_____

(Optional Format 1-2-96)